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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/054,841	01/23/2002	Fang Chen	19999YCA	9080

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MERCK AND CO INC
P O BOX 2000
RAHWAY, NJ 070650907

EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 09/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/054,841	CHEN, FANG	
	Examiner	Art Unit	
	Prema M Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *1-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restriction

1. Applicant's election without traverse of Group II (claims 23-44) on 7/26/2004, is acknowledged.

Claims 1-22 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim objections

2a. Claims 23, 27, 31, and 38, are objected to for the following reason:

There are sequences presented by both SEQ ID NO and the entire sequences themselves in claims. It is suggested that the nucleic acid and amino acid sequences be identified only by the appropriate sequence identifier as set forth in the "Sequence Listing" as required by 37 CFR § 1.821(d). Applicants are requested to remove the recitation of the sequences from the claims and simply recite the SEQ ID NO. Reciting both the SEQ ID NO and the sequences themselves is awkward, difficult to consider and increases the possibility of printer errors.

2b. Claim 30 is objected to for the following reason:

Claim 30, line 6, recites "...of said the human nNR1 protein" which is grammatically incorrect.

Appropriate correction is required.

Claim rejections-35 USC § 101/112, first paragraph

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-44 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance.

It is clear from the instant specification that the protein nuclear receptor nNR1 is what is termed an "orphan receptor" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. On page 35, EXAMPLE 1, Applicants disclose:

Isolation and Characterization of DNA Fragments encoding nNR1 and nNR2. The DNA sequences from several representative subfamilies (Giguère, et 2., 1988, Nature 331: 91-94) were used to query the EST database by using the Blast program. Two ESTs (Genbank accession number h91890 (nNR1) and w26275 (nNR2)) were identified with homology to human ERR2 at DNA sequence level.

However, it is commonly known in the art that sequence-to-function methods of assigning protein function are prone to errors (Doerks et al. 1998). These errors can be due to sequence similarity of the query region to a region of the alleged similar protein that is not the active site, as well as homologs that did not have the same catalytic activity

because active site residues of the characterized family were not conserved (Doerks et al., page 248, column 3, fourth and fifth paragraphs). Inaccurate use of sequence-to-function methods have led to significant function-annotation errors in the sequence databases (Doerks et al. Page 250, column 1, third paragraph). There is little doubt that after complete characterization, this protein will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicants claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson, 148 U.S.P.Q. 689 (Sus. Ct, 1966)*, in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the Court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The Court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a DNA molecule encoding a protein of as yet undetermined function or biological significance. Until some actual and specific significance can be attributed to the protein identified in the specification as nuclear

receptor nNR2, or the DNA encoding it, the instant invention is incomplete. The DNA of the instant invention and the protein encoded thereby are compounds, which are known to be structurally analogous to proteins, which are known in the art as nuclear receptors. In the absence of a knowledge of the natural ligands or biological significance of this protein, there is no immediately obvious "patentable" use for it. To employ a protein of the instant invention in the identification of substances, which inhibit its activity (page 32 of specification) is clearly to use it as the object of further research which has been determined by the Courts to be a non-patentable utility. Since the instant specification does not disclose a "real world" use for the nuclear receptor nNR2, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful. Furthermore, because the claimed invention is not supported by a specific asserted utility for the reasons set forth above, credibility cannot be ascertained.

Claims 23-44 are also rejected under 35 U.S.C. 112, first paragraph, as failing to adequately teach how to use the instant invention. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim rejections-35 USC § 112, first paragraph

4. Claims 25, 29, 35-36, 42-43, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a host cell in culture comprising an expression vector comprising the sequence set forth in SEQ ID NO: 3, does not reasonably provide enablement for *in vivo* transfection.

The specification discloses that the nucleic acids of the current invention can be

expressed in a wide variety of host cell types, including cells within a host animal (page 25). However, there are no actual or prophetic examples that disclose how to make or use host cells that comprise a DNA sequence as set forth in SEQ ID NO: 3 in an animal. The Examiner cites Eck & Wilson (page 8 1, column 2, second paragraph to page 82, column 1, second paragraph) who report that numerous factors complicate *in vivo* gene expression which have not been shown to be overcome by routine experimentation. These include, the fate of the DNA vector itself (volume distribution, rate of clearance into the tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced. Since the instant disclosure does not address any of the methods necessary to make a host cell in an animal, which comprises the polynucleotide of interest, the claims as written are not enabled. This rejection could be overcome by addition of the limitation wherein the host cells are "isolated".

Claim Rejections - 35 USC 112, second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 1 12:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 30, 32-39 are rejected under 35 U.S.C. 1 12, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30 is rejected as vague and indefinite because the limitation "human nNR2 protein" lacks antecedent basis in claim 28, which refers to "human nNR2 protein". Appropriate correction is requested.

Claims 32 and 39 are rejected as vague and indefinite in their recitation of the limitation "about nucleotide...". Even though the use of the term "about" in a claim is inherently vague and indefinite, its use is appropriate when employed to limit a value which is composed of indefinitely divisible units such as inches, meters, grams, and pints, where it is impractical to produce an item, which has exactly the dimension recited. Even if one could practically produce an item, which is exactly 1 inch in length, the length of that item is conditional upon the temperature at which it is measured. However, when defining an invention in terms of indivisible numerical units such as the number of nucleotides in a nucleic acid, the number of amino acids in a polypeptide or the number of legs on a chair or table, the term "about" is unacceptably vague and indefinite since it is practical to employ a term which possesses the required precision. If, for example, it is Applicant's intention that the claims should encompass a nucleic acid comprising from nucleotide 126 to nucleotide 1382 of SEQ ID NO:3 as in claim 32, then this is exactly what the claim should recite. One would not know if the term "about nucleotide 126" would include or exclude nucleotides 120, 125 or even 130.

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can be reached on (571) 272-0961.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
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